

Remarks

Claims 1-20 were pending. Claims 19 and 20 have been withdrawn in response to the Restriction Requirement of October 14, 2005. Claim 14 has been withdrawn by the Office action. Applicants hereby cancel claim 11 and amend independent claims 1 and 16 by incorporating the limitation of claim 11. Applicants further cancel claim 18 without prejudice to Applicants' right to pursue their subject matter in the present application and in related applications.

Upon entry of this amendment, claims 1-10, 12, 13 and 15-17 will be pending and presented for consideration.

Status of Claim 14

In the Reply to Restriction Requirement of November 7, 2005, Applicants elected, with traverse, a) Gene TLR2; b) SEQ ID NO: 1; c) CPS No. 1 (2325-2635 of SEQ ID No: 1); and SEQ ID NO: 240. Although the Office action acknowledged that Applicants' ground of traversal of the above election was persuasive, the Office action proceeded to treat the above election as an election of species and withdrew claim 14 from examination. Applicants respectfully request reconsideration of the withdrawal of claim 14 and request its examination upon determination of the allowability of amended claim 1.

Information Disclosure Statement

Applicants thank Examiner Liu for considering the art from the Information Disclosure Statements of February 20, 2004; April 13, 2004; February 1, 2005; September 2, 2005; and September 19, 2005. However, Applicants note that the examiner has omitted to initial page 2 of 2 of the Information Disclosure Statement of September 2, 2005. Applicants hereby attach a copy of page 2 of 2 of the Information Disclosure Statement of September 2, 2005, and request that Examiner Liu return an initialed copy of said page to Applicants in due course.

Claim Rejections under 35 U.S.C. § 102

The Office action rejected claims 1, 2, 4-7, 9, 10, and 16-18 as allegedly anticipated by U.S. Patent No. 6,190,857 ("Ralph"). The Office action further rejected claims 1-6 and 16-19 as allegedly anticipated by Immunology and Cell Biology, vol. 76: 357-362 (1998), authored by

Olive *et al.* (“Olive”). Applicants have amended the independent claims to incorporate the limitation of claim 11 as previously pending. Applicants note that claim 11 was not rejected under 35 U.S.C. § 102. Accordingly, Applicants request reconsideration and withdrawal of the rejections in view of the amended claims.

Claim Rejections under 35 U.S.C. § 103 over Ralph in view of Golub

The Office action rejected claims 1-10 and 15-18 as allegedly obvious over Ralph in view of Science, vol. 286: 531-537 (1999), authored by Golub *et al.* (“Golub”). Applicants submit that these rejections have been rendered moot by the present amendments to claims 1 and 16, in particular, the incorporation of the limitations of previously pending claim 11 into claims 1 and 16. Accordingly, reconsideration and withdrawal of these rejections are requested.

Claim Rejections under 35 U.S.C. § 103 over Ralph in view of Liu

The Office action further rejected claims 1, 2, 4-7, 9-13 and 16-18 as allegedly obvious over Ralph in view of Infection and Immunity, vol. 69: 2788-2796 (2001), authored by Liu *et al.* (“Liu”). Applicants respectfully traverse these rejections.

The appropriate criteria for the determination of obviousness under 35 U.S.C. § 103 is whether the prior art would have suggested to one of ordinary skill in the art that the claimed subject matter should be carried out and would have a reasonable likelihood of success. Both the suggestion and the expectation of success must be found in the prior art, not in Applicant’s disclosure. *In re Dow Chemical Company*, 837 F.2d 469,473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). That is, obviousness cannot be established by combining the teachings of the prior art to produce claimed invention, absent some teaching or suggestion or incentive in the art supporting the combination. *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Cited references which merely indicate the isolated elements recited in the claims are not a sufficient basis for concluding that the combination would have been obvious. *Ex parte Hiyamaizu*, 10 U.S.P.Q.2d 1393 (BPAI 1988).

The Office action acknowledged that Ralph does not specifically teach using TLR2 in his diagnostic method. Ralph also fails to teach or suggest comparing the expression profiles of any of the other genes listed in Table 4 or Table 6 in peripheral blood samples between patients with

a solid tumor or a non-blood disease and disease-free humans as required by amended claims 1 and 16. In attempt to cure the deficiencies of Ralph, the Office action cited Liu to provide disclosure of TLR2 and alleged that because Ralph teaches that the “immune system is an attractive choice to survey because it would be expected to respond robustly to a malignant disease process,” an ordinary skilled artisan would be motivated to compare TLR2 gene expression profile from samples obtained from diseased and healthy individuals (pp. 9-10 of the Office action).

Applicants submit that there is no motivation to combine the teachings of Ralph and Liu to arrive at the Applicants’ claimed invention. “Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art.” M.P.E.P. § 2143.01(I). Ralph’s teaching that “the immune system is an attractive choice to survey” does not amount to a motivation to specifically select TLR2, or any other gene from Table 4 or Table 6, from the thousands of genes expressed in PBMCs when comparing an expression profile in a peripheral blood sample to a reference expression profile. Similarly, Liu’s disclosure of TLR2 as involved in immune signaling and expressed in PBMCs does not amount to a specific motivation to select TLR2, or any other gene from Table 4 or Table 6, for use in the claimed invention. In the absence of a teaching, suggestion, or motivation to select TLR2 or any other gene from Table 4 or Table 6 for use in the claimed invention, the cited references cannot render the claimed invention obvious.

Furthermore, Ralph’s statement that the immune system is “an attractive choice to survey” is at best an invitation to experiment which, absent a reasonable likelihood of success, cannot properly support a rejection under section 103. See *In re Dow Chemical Co.*, 837 F.2d 469 (Fed. Cir. 1988) and *In re Eli Lilly & Co.*, 902 F.2d 943 (Fed. Cir. 1990). Ralph did not identify TLR2 or any other gene listed in Tables 4 and 6 as useful in the claimed method. Indeed, of the thousands of genes expressed in peripheral blood, Ralph identified few genes that actually demonstrate differential expression in the peripheral blood of prostate cancer patients when compared with disease-free humans. Given that Ralph identified relatively few genes to be useful, and Liu failed to provide any reasonable basis for concluding that TLR2 (or any other


gene listed in Tables 4 and 6) would be specifically useful, Applicants submit that a person of ordinary skill in the art would not have had the requisite expectation that s/he could successfully practice Applicants' claimed invention.

Since the requisite expectation of success cannot be found in the combined teachings of Ralph and Liu, Applicants submit that their combination does not render independent claims 1 and 16 and their respective dependent claims obvious. Reconsideration and withdrawal of the rejections are requested.

CONCLUSION

Upon entry of this amendment, claims 1-10, 12, 13 and 15-17 will be pending and presented for consideration. Applicants believe the claims to be in condition for allowance and request a telephonic interview with the undersigned attorney to address any outstanding issues.

Respectfully submitted,



Brian Fairchild, Ph.D.
Attorney for Applicant
Kirkpatrick & Lockhart Nicholson
Graham LLP
75 State Street
Boston, Massachusetts 02109-1808

Date: March 7, 2006
Reg. No. 48,645

Tel. No.: (617) 261-3169
Fax No.: (617) 261-3175